National Research Ethics Committee

NREC-CT Meeting

05 June 2024

Attendance

Name	Role
Prof Mary Donnelly	Chairperson, NREC-CT C
Prof John Faul	Deputy Chairperson, NREC-CT C
Dr Jean Saunders	Deputy Chairperson, NREC-CT C
Prof Austin Duffy	Committee Member, NREC-CT C
Prof Fionnuala Breathnach	Committee Member, NREC-CT C
Dr Susan Finnerty	Committee Member, NREC-CT C
Prof Andrew Smyth	Committee Member, NREC-CT C
Dr Steve Meaney	Committee Member, NREC-CT C
Ms Susan Kelly	Committee Member, NREC-CT C
Dr Deborah Wallace	Committee Member, NREC-CT C
Ms Paula Prendeville	Committee Member, NREC-CT C
Mr Gerry Eastwood	Committee Member, NREC-CT C
Prof Anne Mathews	Committee Member, NREC-CT C
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Dr Emily Vereker	Head of Office, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs

Apologies: Mr Philip Berman, Dr Dervla Kelly

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-513087-26-00
- 22-NREC-CT-173_Mod-4
- 2022-502705-15-00 SM1
- 22-NREC-CT-012_Mod-6
- 22-NREC-CT-157_Mod-5
- 22-NREC-CT-126_Mod-2
- 22-NREC-CT-090_Mod-2
- AOB

- The Chair welcomed the NREC-CT C.
  - The minutes from the previous NREC-CT C meeting on 01 May 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-513087-26-00

Institutions: Beaumont Hospital, St James's Hospital, University Hospital Galway

Study title: A Randomized, Controlled, Multiregional Phase 3 Study of Ivonescimab Combined with Chemotherapy Versus Pembrolizumab Combined with Chemotherapy for the First-line Treatment of Metastatic Squamous Non-small Cell Lung Cancer (HARMONi-3)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part II Considerations

- **Compliance with national requirements on data protection**
- No Considerations
- **Compliance with use of biological samples**
- The NREC-CT requested that the Compliance with Member State applicable rules for the collection, storage and future use of human biological samples form is updated to align with requested changes in the PISCF regarding future use of samples / data and genetic research.
- The NREC-CT noted that unsolicited findings will be reported to the investigator who will then inform the participants. The NREC-CT requested additional information around the processes and safeguards in place to protect and support participants. They also query whether participants be offered the opportunity to opt-out from receiving unsolicited findings if they choose to.
- **Financial arrangements**
- No Considerations
- **Proof of insurance**
- The NREC-CT noted that the insurance certificate expires in 2026 and requested confirmation that insurance is in place for the duration of the trial.
- **Recruitment arrangements**
- No Considerations
- **Subject information and informed consent form**
- The NREC-CT noted that the Summary PISCF is not presented in a participant friendly and informative format and requested that the Summary PISCF is revised to highlight the pertinent issues that trial participation will involve in a clear and accessible format, using plain English suitable for a lay audience. This NREC guide may be useful: https://www.nrecoffice.ie/pil-summary-guidance/. Please also address the following:
    - The NREC-CT noted that pg. 2. of the PISCF states that if participants decide not to participate in the trial or decide to leave the trial 'it won't be held against you' and requested that this wording is revised to be more patient friendly and informative.

    - The NREC-CT requested that the section under the heading 'what should I know about this research' on pg. 2 of the PISCF is revised to be more patient-friendly, clearer and simplified into plain language for a lay audience.
- The NREC-CT deemed the Main PISCF document as inadequate, as they do not provide the required clear and accessible information for participants to make a fully informed decision about participating in the trial in line with ICH-GCP. The NREC-CT requested that the PISCF documents are thoroughly revised to ensure that information is presented in a clear and accessible format, using plain English suitable for a lay audience.
- The NREC-CT requested that the following issues are addressed in revising the Main PISCF
    - The NREC-CT requested that the phrase 'penalty / loss of benefits…' on pg. 4 of the PISCF is replaced with 'clinical care or routine care'.
    - The NREC-CT requested that either the term 'investigational new drug' or 'study drug' throughout the PISCF, as the use of both terms is potentially confusing for participants.
    - The NREC-CT requested that the phrase 'the study drug is carefully made' on pg. 4 of the PISCF is clarified.
    - The NREC-CT noted that the section 'How long will be I be in this research' on pg. 4 of the PISCF is poorly written and lacks clarity and requested that this section is revised so participants are fully informed.
    - The NREC-CT requested that pg. 5 of the PISCF includes details of what the 'screening tests' are, or provides reference to the table which follows on pg. 6.
    - The NREC-CT noted that the section 'What happens to me if I agree to take part in this research?' on pg. 5 of the PISCF is overly long and potentially difficult to understand and requested that the section is fully revised to be more patient friendly and describe the study in a clear concise manner using plain English suitable for a lay audience (suggest that a more general overview followed by the tables might be beneficial and easier to understand).
        - Please also list the chemotherapy drugs again for Arm B, and remove reference to Arm A, when describing Arm B.
    - The NREC-CT noted that pgs. 10-23 of the PISCF provide an extensive list of IMP potential side effects and requested that these are provided in a more patient friendly format.
    - The NREC-CT requested that the phrase 'while you are in this study you still need to get regular medical care', on pg. 26 of the PISCF is reworded, as it is potentially confusing for participants.
    - The NREC-CT noted that pg. 27 of the PISCF states 'What other choices...' and questioned the relevance of this statement. Please provide clarification that SoC is provided to anyone choosing not to participate in the trial.
    - The NREC-CT noted the reference to 'alternative treatments' on pg. 35 of the PISCF. Please clarify in the PISCF if this statement refers to SoC.
    - The NREC-CT requested that the statements 'you are unable to keep your scheduled appointments' and 'discretion of the investigator' in the section

'Can I be removed from the research without my approval?' on pg. 32 of the PISCF are clarified.

- The NREC-CT noted that participants are to undergo testing for biomarker analysis on pg. 8 of the PISCF and requested that detail is added as to why these samples are being taken and what type of analysis will be performed (i.e. genetic, proteomic etc.). This should be explained using plain English suitable for a lay audience.
- The NREC-CT noted that pg. 9 of the PISCF states 'you must inform your study doctor immediately if you experience any unusual symptoms or side effects during the study' and requested that a list of potentially unusual symptoms or side effects is listed. This should be included in the following section where they refer to 'reporting any issues that bother you'.
- The NREC-CT notes that pg. 18 of the PISCF advises participants if they were experiencing the serious side effect of 'tumour lysis syndrome' to tell their doctor straight away and requested that this is revised to include additional information on how a participant may determine that they are experiencing tumour lysis syndrome.
- The NREC-CT noted the statement 'If your cancer is not evaluated for specific gene alterations, you may be missing out on potential therapies that are Health Products Regulatory Authority (HPRA)-approved specifically for these alterations (including therapies that target EGFR mutations, ALK rearrangements, or ROS1 rearrangement)' on pg. 27 of the Main PISCF and requested that this is statement is revised, as it may be interpreted that participants will be at a disadvantage if they do not participate in the trial.
- The NREC-CT noted that pg. 27 of the Main PISCF and pg. 3 of the Pregnancy PISCF state that participant information may be stored for 'at least 25 years' after completion of the trial and requested that the maximum length of time participants data will be retained for is clearly stated in the PISCF documents.
- The NREC-CT noted that pg. 28 of the PISCF states data will be shared with 'Sponsors partners and affiliates', and requested that a full list of Sponsors partners and affiliates is listed, and detail is provided as to what data will be shared.
- The NREC-CT noted that 28 of the Main PISCF and pg. 4 of the Pregnancy PISCF state that NREC may have access to participants medical record / identifiable information and requested that this text is amended to state that that NREC will only have access to non-identifiable data, and not participant's personal data.
- The NREC-CT noted that pg. 28 of the Main PISCF states 'Further, the Sponsor may be required to disclose your personal data in response to lawful requests by public authorities, including those to meet national security or law enforcement requirements' and requested that it is clarified in the PISCF so participants are fully information what data would be shared in this instance and under what circumstances this data would be shared.
- The NREC-CT requested that the text related to optional future research on pg. 31 of the Main PISCF is explicit and distinct from main text of the PISCF and is incorporated into the separate Optional Future Research consent section on pg. 39 of the Main PISCF.
    - The NREC-CT requested that confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

- The NREC-CT requested that the statement regarding genetic aberrations 'information that are known or suspected to have a link with your cancer and / or drug treatments' on pg. 30 of the Main PISCF is clarified so participants are fully informed.
- The NREC-CT requested that clarity is provided in the PISCF regarding genetic testing and requested the following:
    - It should be made clear to participants whether these tests are optional or mandatory
    - The genetic testing requested must be restricted and defined in line with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) and clearly explained clearly to the participant,
    - Explicit consent should be obtained for genetic testing
    - Clarification should be provided on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data. For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- **Suitability of the clinical trial sites facilities**
- No Considerations
- **Suitability of the investigator**
- The NREC-CT requested that evidence of up-to-date ICH-GCP is provided for Dr [redacted]

2022-502705-15-00 SM1

Institutions: Cork University Hospital, Tallaght University Hospital

Study title: A Phase III, Double-blind, Multicenter, Randomized study of Atezolizumab (anti-PD-L1 antibody) versus Placebo as Adjuvant therapy in Patients with High-Risk Muscle-Invasive Bladder Cancer who are CTDNA positive following cystectomy

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part II Considerations

- **Subject information and informed consent form**

- The NREC-CT requested that the term 'ECOG performance status' is explained using plain English suitable for a lay audience on pg. 3 of the Treatment PISCF and pg. 5 of the Surveillance PISCF.
- The NREC-CT noted that the screening test involves the use of an experimental test ([redacted]) and requested the following:
    - It is explained to participants in more detail in the Pre-Screening PISCF that while this test is experimental in the context of invasive bladder cancer, it has been shown to be highly effective at identifying patients at risk of cancer recurrence when used in the setting of other cancers.
    - Confirmation that approval for the experimental test ([redacted] will be obtained under the In Vitro Diagnostic Medical Devices Regulations IVDR; EU No 2017/746, if required, before recruitment to the trial.
- The NREC-CT noted on pg. 11 of the Pre-Screening PISCF, pg. 22 /23 of the Treatment PISCF and pg. 14 of the Surveillance PISCF is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof' (i.e. bladder cancer) and this is clearly stated in the main body and informed consent section of the PISCF documents. The NREC-CT requested the following:
    - i) that consent for future use of samples is provided on a separate consent form and not bundled (a tick box for participant initials should be provided along each consent item)
    - ii) is made optional
    - iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - Confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that pg. 2 of the Pre-screening PISCF, pg. 22/23 of the Treatment PISCF and pg. 14 of the Surveillance PISCF state that participants may undergo whole exome / whole genome sequencing and requested the following:
    - Whole exome /whole genome sequencing is confined to genes involved in the disease being treated (i.e. bladder cancer) and /or genes involved in the metabolism of the medicines being used in the trial and this is explained in the PISCF.
    - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the PISCF.
    - The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
    - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.
    - Clarification is provided in the PISCF on the mechanism for anonymisation, storage and security and transfer of genetic material and

its associated data. For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf

- Confirmation that appropriate supports are in place for genetic counselling, should it be required.

- The NREC-CT noted that pg. 12 of the Pre-Screening PISCF, pg. 24 of the Treatment PISCF and pg. 15 of the Surveillance PISCF state that the ethics committee may have access to participants medical record / identifiable information and requested that this text is amended to state that that NREC will only have access to non-identifiable data, and not participant's personal data.
- The NREC-CT noted the use of the term 'legally authorized representative' throughout the PISCFs. As there is no legal basis for this term under Irish law, the Committee requested that it is removed or amended in line with national legislation

22-NREC-CT-173_Mod-4

Institutions: Beaumont Hospital

Study title: Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response directed definitive therapy in early stage HER2-positive breast cancer: a standard chemotherapy-sparing approach to curative intent treatment – SHAMROCK study

- **NREC-CT Decision:**

- Favourable

22-NREC-CT-012_Mod-6

Institutions: St Vincent's University Hospital

Study title: A Randomized, Blinded, Placebo-controlled, Phase 2 Study of INBRX-109 in Unresectable or Metastatic Conventional Chondrosarcoma

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that pg. 3 of the Main PISCF ('At the end of the study we will save some of the data in case we need to check it and for future research') is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to 'specified health research, either in relation to a particular area or more generally in that area or a related area of

health research, or part thereof' (i.e. Chondrosarcoma) and this is clearly stated in the main body and informed consent section of the PISCF. The NREC-CT requested the following:

- i) that consent for future use of samples is provided on a separate consent form and not bundled (a tick box for participant initials should be provided along each consent item)
- ii) is made optional
- iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
- The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

22-NREC-CT-157_Mod-5

Institutions: Sheaf House, Tallaght Adult Mental Health Services

Study title: A randomized, double-blind, placebo-controlled, Phase 2b trial with an open-label extension to determine the safety and efficacy of GH001 in patients with treatment-resistant depression

- **NREC-CT Decision:**

- Favourable

22-NREC-CT-126_Mod-2

Institutions: Meath Hospital incorporating the National Children's Hospital (AMNCH)

Tallaght DUBLIN

Study title: A prospective randomised phase III study of androgen deprivation therapy with or without docetaxel with or without local radiotherapy with or without abiraterone acetate and prednisone in patients with metastatic hormone-naïve prostate cancer

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that the Patient Information Letter is not written in a participant friendly manner, is ambiguous in places and uses technical language. The NREC-CT requested that this letter is revised to be more participant-friendly, clearer and simplified into plain English for a lay audience, and that a thorough check of the text is carried out to eliminate ambiguity created by use of less specific language. Specific points that were highlighted are as follows:
  - The NREC-CT noted that the reference to previous information communicated to participants (i.e. on pg. 1 of the Participant Information

Letter) is bureaucratic in tone and requested that this is revised to be more accessible and participant-facing.
    - The NREC-CT requested that clear guidance is provided to participants detailing what actions, if any, need to be taken by participants, on receipt of this letter, in particular in relation to any potential requirements related to availability of the study drug (*c.f.* below) and the continuity of their care.
    - The NREC-CT requested that the phrase 'You are taking part in…' on pg. 1 of the Letter is rephrased to emphasize the nature of participation in the study, i.e. 'You are a participant in…'
    - The NREC-CT noted that the statement 'The main questions posed by this clinical study (primary endpoint) were communicated to the scientific community at medical conferences in 2021 and 2023' on pg. 1 of the Participant Information Letter is clarified, as it would be expected that the outcomes of the trial were of most interest to the scientific community, rather than the main questions.
    - The NREC-CT requested that the phrase 'there is no longer any need for further research' on pg. 1 of the Participant Information Letter is ambiguous and requires further clarification as to whether this relates only to the current study.
    - The NREC-CT noted that that pg. 1 of the Participant Information Letter states that 'an end-of-treatment visit will be scheduled 4 weeks after the last dose of treatment' and requested clarification is provided as to whether this relates to the last dose of treatment as per original protocol or the updated protocol (end of study).
- The NREC-CT required clarification in relation to the continued availability of the study drug (abiraterone acetate) for participants, should it be clinically necessary, once the trial has ended.

22-NREC-CT-090_Mod-2

Institutions: Cork University Hospital

Study title: ATLAS - A randomized, double-blind, placebo-controlled study assessing the long-term effect of dupilumab on prevention of lung function decline in patients with uncontrolled moderate to severe asthma

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that it is not clear on pg. 11 of the PISCF whether the analysis is complete on the samples already collected for the discontinued pharmacogenetic/biomarker studies and requested that this is clarified for participants in the PISCF.

- The NREC-CT noted that the protocol states that 'samples already collected will be analyzed' for optional biomarkers and that 'samples collected…will be analyzed' for Sub study 8.5.3. and requested clarification as to why these samples are being retained as the optional pharmacogenetic/biomarker sample collection is being discontinued.
    - The NREC-CT requested that it is explained to participants in the PISCF what will happen to their retained samples.
- The NREC-CT noted that rationale for not continuing the optional sub-studies is not explained to participants on pg. 11 of the PISCF and requested that a clear rationale is provided for participants in the PISCF
- It is not clear in the PISCF if any genetic tests will be conducted on samples, if the optional pharmacogenetic/biomarker sample collection, and associated studies, are discontinued. The NREC-CT requested that if genetic tests are being carried out, then this should be clearly explained in the PISCF. The NREC-CT requested the following:
    - It should be made clear to participants whether these tests are optional or mandatory
    - The genetic testing requested must be restricted and defined in line with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) and explained clearly to the participant,
    - Explicit consent should be obtained for genetic testing
    - Clarification should be provided on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data. For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT noted on pg. 20 of the PISCF is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof' (i.e. asthma) and this is clearly stated in the main body and informed consent section of the PISCF documents. The NREC-CT requested the following:
    - i) that consent for future use of samples is provided on a separate consent form and not bundled (a tick box for participant initials should be provided along each consent item)
    - ii) is made optional
    - iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.

    - Confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted conflicting information in the PISCF regarding maximum retention periods for data - PISCF pg. 11 states ‘Your data will be stored for 25 years after the end of the study or more if required by regulations’ whereas pg. 25 states ‘Your data will be kept for at least 25 years from the end of the study’. The NREC-CT requested that the maximum length of time data be retained for, is clearly stated in the PISCF.
- The NREC-CT recommended that the changes made to the PISCF would benefit from a PISCF addendum outlining the rationale for the changes to the sample collection practices.

- AOB: N/A